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Mutation testing recommended for advanced and refractory thyroid cancer

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FROM HEAD & NECK

A new consensus statement from the American Head and Neck Society Endocrine Surgery Section and International Thyroid Oncology Group focuses on a definition of advanced thyroid cancer and outlines strategies for mutation testing and targeted treatment.

Mutation testing should not be pursued if cancer burden and disease threat is low, since most thyroid cancers have a very good prognosis and are highly treatable. But 15% of differentiated thyroid cancer cases are locally advanced, and radioiodine refractory differentiated thyroid cancer has a 10-year survival below 50%.

More generally, advanced thyroid cancer has not been well defined clinically. Physicians with experience diagnosing advanced disease may recognize it, but there is no widely accepted definition. “This may be the first time that an expert group of physicians has attempted to define what advanced thyroid cancer is,” said David Shonka, MD, <https://uvahealth.com/findadoctor/profile/david-charles-shonka-jr> who is a coauthor of the consensus statement, which was published online <https://pubmed.ncbi.nlm.nih.gov/35274388/> in Head & Neck. He is an associate professor of otolaryngology/head and neck surgery at the University of Virginia, Charlottesville.

mutational testing," the authors wrote. "Next-generation sequencing can reveal targetable mutations and potentially give patients affected by advanced thyroid carcinoma systemic treatment options that can prolong survival. These new innovative approaches are changing the landscape of clinical care for patients with advanced thyroid cancer."

For differentiated thyroid cancer and medullary thyroid carcinoma, the authors created a definition that combines structural factors on imaging, along with surgical findings, and biochemical, histologic, and molecular factors. Anaplastic thyroid cancer should always be considered advanced, even after a complete resection and incidental pathological identification.

The statement also summarizes recent advances in thyroid cancer that have revealed molecular markers which contribute to oncogenesis. Initially, those approaches were applied to indeterminate fine needle biopsies to improve diagnosis. More recent studies used them to match patients to targeted therapies. There are Food and Drug Administration–approved therapies targeting the BRAF and RET mutations, but advanced thyroid cancer is also included in some "basket" trials that test targeted agents against driver mutations across multiple tumor types.

Radioiodine refractory differentiated thyroid cancer had few treatments as recently as 10 years ago. But recent research has shown that multikinase inhibitors improve outcomes, and a range of mutations have been found in this type of thyroid cancer, including BRAF V600E, RET, PIK3CA, and PTEN, and fusions involving RET, NTRK, and ALK. Other mutations have been linked to more aggressive disease. Efforts to personalize treatment also include microsatellite stability status, tumor mutational burden, and programmed death–ligand 1 status as indicators for immunotherapy. "With discovery of many

thyroid cancer have comprehensive genomic profiling on tumor tissue through (next generation sequencing)," the authors wrote.

These newer and novel therapies have presented physicians with options outside of surgery, chemotherapy, or radiotherapy, which have low efficacy against advanced thyroid cancer. "It is an area in which there has been substantial change. Even 5-7 years ago, patients with advanced thyroid cancer that was not responsive to radioactive iodine or surgery really didn't have a lot of options. This is a really an exciting and growing field," Dr. Shonka said.

He specifically cited anaplastic thyroid cancer, which like radioiodine refractory differentiated thyroid cancer has had few treatment options until recently. "Now, if you see a patient with anaplastic thyroid cancer, your knee-jerk reaction should be 'let's do molecular testing on this, this is definitely advanced disease.' If they have a BRAF mutation, that's targetable, and we can treat this patient with combination therapy that actually improves their survival. So, there's some exciting stuff happening and probably more coming down the road as we develop new drugs that can target these mutations that we're identifying."

Dr. Shonka has no relevant financial disclosures.